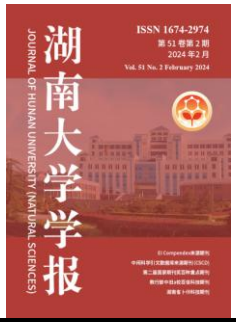

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Diabetes Mellitus Comorbid with Metabolic Syndrome in New Karachi Township: Prevalence, Risk Analysis, and Future Perspectives

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Abstract: This study aimed to determine the prevalence of metabolic syndrome in known diabetic patients attending diabetes outpatient departments in a tertiary care hospital and to determine the effect of its presence on different body parameters and risk of diabetic complications. This is the first study conducted in the target population of New Karachi Township. Diabetes mellitus correlates with insulin resistance, which results in the development of metabolic syndrome, thus contributing to diabetic complications. This cross-sectional study involved purposive sampling in a tertiary care hospital for 17 months. The ethical committee of the government hospital approved the protocol. After obtaining the consent, participants were interviewed, examined, and asked for blood and urine samples after 14 hours. The prevalence of metabolic syndrome in known diabetic patients was 60%, with body mass index ($p < 0.05$), blood pressure ($p < 0.001$), triglycerides ($p < 0.001$), and fasting sugar ($p < 0.05$) as positive risk factors and female preponderance. Metabolic syndrome was an independent risk factor for diabetic neuropathy ($p = 0.005$) and nephropathy ($p = 0.014$). The metabolic syndrome relates to diabetes mellitus, and developing this correlation in the Pakistani population at large scale study along with proper counseling and awareness campaigns are of utmost importance. The government should take efficient measures to improve the living standards of the low-income group.

Keywords: diabetes mellitus, complications, metabolic syndrome, cross-sectional study.

卡拉奇新鎮糖尿病合併代謝症候群：盛行率、風險分析與未來展望

摘要：本研究旨在確定三級醫院糖尿病門診的已知糖尿病患者中代謝症候群的盛行率，並確定其存在對不同身體參數和糖尿病併發症風險的影響。這是針對新卡拉奇鎮目標族群的第一項研究。糖尿病與胰島素抗性相關，胰島素阻抗會導致代謝症候群的發生，進而導致糖尿病併發症。這項橫斷面研究在一家三級醫院進行了 17 個月的有目的的抽樣。政府醫院倫理委員會批准了該方案。獲得同意後，14 小時後對參與者進行訪談、檢查並要求血液和尿液樣本。已知糖尿病患者中代謝症候群的盛行率為 60%，體重指數($p < 0.05$)、血壓($p < 0.001$)、三酸甘油酯($p < 0.001$) 和空腹血糖($p < 0.05$) 為陽性危險因素和女性佔優勢。代謝症候群是糖尿病神經病變（$p = 0.005$）和腎臟病（$p = 0.014$）的獨立危險因子。代謝症候群與糖尿病有關，在巴基斯坦人群中進行大規模研究以發展這種相關性以及適當的諮詢和宣傳活動至關

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重要。政府應採取有效措施，提高低收入群體的生活水準。

关键词：糖尿病、併發症、代謝症候群、橫斷面研究。

1. Introduction

Diabetes mellitus is a metabolic disorder diagnosed according to the American Diabetes Association, when a patient presents with polyurea, polydipsia, and polyuria along with FBS > 126 mg/dl and HbA1c > 6.5%. Type II diabetes mellitus is associated with insulin resistance and burning of the β – cells of pancreatic islets [1]. This same insulin resistance also leads to another disorder known as "metabolic syndrome" [2, 3].

Metabolic syndrome is a deadly quartet of central and abdominal obesity, hypertension, insulin resistance, and dyslipidemia [2, 4]. On an independent basis, metabolic syndrome is a proinflammatory condition generated due to excessive fatty flux, which contributes to insulin resistance and increases the risk of diabetes and hypertension [3]. The major contributing factor for metabolic syndrome is obesity [5], which contributes a direct proportion to metabolic syndrome prevalence [6].

The prevalence of metabolic syndrome in diabetic patients ranges from 10% to 84% in different regions [7], which is increasing to an alarming level with an increase in obesity [8-10]. This study aimed to determine the prevalence of metabolic syndrome in known diabetic patients attending a diabetes outpatient department (OPD) in a tertiary care hospital and to determine the effect of its presence on different body parameters and the risk of microvascular complications.

2. Materials and Methods

2.1. Study Design

An interviewer operated questionnaire-based "cross – sectional study" that was conducted in a local tertiary care hospital for 17 months.

2.2. Sampling

A total of 600 patients were contacted for the study, out of which 308 responded, thus providing a response rate of 51%. Patients randomly contacted with persons who were attending diabetes OPD with diabetes mellitus for more than 5 years. The ethical committee of the government hospital with ref number SGHNK/922 [11] approved the protocol.

As mentioned by [11], with 10% frequency and 99% confidence, the sample size was calculated as 235 from the online sample size calculator [12].

2.3. Diagnostic Criteria

Metabolic syndrome is also termed insulin resistance syndrome [2, 13]. As the present sample was already known diabetic patients, all participants fulfilled one criteria of hyperglycemia. They were categorized in the metabolic syndrome group when they met two or more [14] of the following criteria: "body mass index" more than 30, blood pressure 130/85 mmHg, "triglycerides" greater than 150 mg/dl, "high density lipoprotein" 45, and "urinary albumin creatinine ratio" greater than 30 mg/g of creatinine [15].

2.4. Data Collection

After conducting the interview with the participants of the study, data were collected by measuring BP (Corteza ®, Germany) and height and weight (Health scale, China). Patients were asked to submit their blood and urine samples the next day to the diagnostic laboratory of the hospital the next day after 12–14 h of fasting. Random and fasting blood glucose, HbA1c, lipid profile, and kidney profile were measured using Vitalab ® (Selectra E automated analyzer, USA).

2.5. Interpretation Using Formulas

After retrieving data, further calculations were performed using the following formulas. Body mass index (BMI) was calculated using weight (kg)/height^2 (meter^2) [16]. Estimated glomerular filtration rate (eGFR) was calculated using "Cockroft-Gault formula" [17], which is (140 – age)×weight (kg)/P_{Cr}72 0.85 (for females). The urinary albumin–creatinine ratio in the first morning void [18] was computed by UACR (mg/g Cr) = U. Albumin (md/dl)/Urinary creatinine (g/dl) [19]. The cholesterol – HDL ratio is an important parameter to check coronary artery disease risk. Therefore, it was calculated as CHR = Chol/HDL [20]. Result interpretation was done by the value ranges mentioned in Table 1.

Table 1 Diagnostic criteria for various variables (The authors)

Classification of weight status of the basis of BMI		
1.	Under weight	< 18.5
2.	Normal	18.5 – 24.9
3.	Over weight	25 – 29.9
4.	Obesity I	30 – 34.9
5.	Obesity II	35 – 39.9
6.	Obesity III	> 40
Classification of Albuminuria		
1.	< 30 mg/g Cr	Normal
2.	30 – 300 mg/g Cr	Micro-albuminuria
3.	> 300 MG/G Cr	Macro-albuminuria
Severity classification of Chol: HDL ratio		
1.	< 3.5	Ideal / very good
2.	3.5 – 5	Should me maintained
3.	> 5	High risk

2.6. Data Analysis

Continuous variables of the data were expressed as avg ± SD and were further analyzed by two-sample unpaired Student's t-test. Categorical variables were expressed as frequency and percentage. It was further analyzed by "Pearson's chi- square test" of correlation. Additional calculation of OR was also conducted using the standard formula of the same.

Logistic regression analysis for the "presence of metabolic syndrome" as a binary variable on the data was performed to identify the effect of age, systolic BP, fasting blood glucose, body mass index, triacylglycerol, cholesterol, LDL, HDL, Chol-HDL ratio, serum creatinine, UACR, nephropathy, and neuropathy as individual covariates.

The result was considered significant when $p < 0.05$. All statistical analyses were conducted using SPSS–20 (SPSS Inc, Chicago, IL, USA).

3. Results

3.1. Demographic Data

With all the patients known to be diabetic for more than five years, 60% of the study population was found to have metabolic syndrome ($\chi^2 = 6.65$, $p = 0.01$). The highest frequency of metabolic syndrome (MS) was found in individuals aged 31–60 years ($\chi^2 = 95.19$, $p < 0.005$), with the average age of the MS-positive group being 48.6 years ($t = -2.98$, $p = 0.003$). Female preponderance was observed (49.4% of total, $\chi^2 = 9.57$, $p = 0.002$) with strong dependency on BMI ($x = 27.76$, $t = 5.03$, $p < 0.05$).

3.2. Systematic Review

Questions regarding weight perception, health status, appetite, and sleep patterns were asked. All of the questions leaving a few questions were not found to be significantly dependent on the presence of MS. However, a few variables discussed below were found to significantly depend on the presence of metabolic syndrome (Table 2).

100% of the metabolic syndrome positive group was found to fatigue easily ($\chi^2 = 4.67$, $p = 0.031$), 69% (n = 128) had a complaint of vertigo ($\chi^2 = 10.41$, $p = 0.001$), out of whom 39% (n = 72) had a history of fall ($\chi^2 = 4.172$, $p = 0.041$) as well as heavy headedness in 52% (n = 160) participants ($\chi^2 = 12.99$, $p < 0.001$). 58% (n = 178) patients presented joint pain, which was significantly correlated to metabolic syndrome ($\chi^2 = 5.21$, $p = 0.022$).

Signs of painful neuropathy were discussed with patients in whom tingling ($\chi^2 = 0.41$, $p = 0.524$) and numbness ($\chi^2 = 0.169$, $p = 0.681$) were not found to be dependent on metabolic syndrome. On the other hand, burning sensation (n = 156, 51%) was found to be significantly dependent on metabolic syndrome ($\chi^2 = 5.82$, $p = 0.016$).

The atherogenic index significantly depended on metabolic syndrome ($\chi^2 = 4.99$, $p = 0.026$). Delayed wound healing was also dependent on the presence of metabolic syndrome in those who presented with the complaint ($\chi^2 = 4.26$, $p = 0.039$).

3.3. Blood Parameters

Blood pressure of the patients was found to be significantly dependent upon the presence of metabolic syndrome (131/87 mmHg vs. 121/80 mmHg, $t = 3.4$ and 4.1 respectively, $p < 0.001$). Fasting (203 vs. 169 mg/dl, $t = 2.27$, $p < 0.025$) and random (290 vs. 256 mg/dl, $t = 1.98$, $p < 0.05$) glucose levels were also found to be significantly dependent on the presence of metabolic syndrome (Table 3).

In the case of lipid profile, only triacylglycerol levels were found to be dependent on metabolic syndrome (192 vs. 146 mg/dl, $t = 3.37$, $p < 0.001$). The log value of TG/HDL, which is termed as the atherogenic index, was found to be above the normal range in both the groups, but the difference between the groups was found to be significant (0.61 vs. 0.43, $t = 5.74$, $p < 0.01$). The atherogenic index when segregated into high-risk and low-risk groups showed strong dependence on the presence of metabolic syndrome ($\chi^2 = 4.99$, $p = 0.026$).

The kidney profile showed that urinary microalbumin levels were strongly dependent on metabolic syndrome (31 vs. 25, $u = 2110$, $p < 0.05$). The urinary albumin– creatinine ratio was also found to be significantly dependent upon metabolic syndrome (75.64 vs. 56.77, $u = 1892$, $p < 0.001$), although both groups were found to be above the normal range, but the difference between the groups was found to be significant.

Table 2 Variables related to systemic review (The authors)

Variable	Response	Metabolic syndrome		χ^2 / p value	Odds Ratio
		Yes	No		
Fatigue	Yes	186	116	4.69	4.76
	No	0	6	$P = 0.031$	
Vertigo	Yes	128	52	10.41	2.97
	No	58	70	$P = 0.001$	
Fall	Yes	72	28	4.172	2.12
	No	114	94	$P = 0.041$	
Heavy	Yes	160	74	12.99	3.99
Headedness	No	26	48	$P < 0.001$	
Joint Pain	Yes	178	104	5.21	3.85

	No	8	18	$P = 0.022$	
Burning	Yes	156	82	5.82	2.54
	No	30	40	$P = 0.016$	
Tingling	Yes	154	96	0.41	1.3
	No	32	26	NS	
Numbness	Yes	160	102	0.169	1.21
	No	26	20	NS	
Delayed wound healing	Yes	58	20	4.26	2.31
	No	128	102	$p = 0.039$	
Cholesterol/HDL ratio	Low/intermediate (< 5)	172	114	0.052	1.15
	High Risk (> 5)	14	8	$p = 0.819$	
Athrogenic Index	High	184	112	4.99	8.21
	Intermediate/Low	2	10	$p = 0.026$	

Table 3 Numerical variables related to metabolic syndrome (The authors)

Variable	**Metabolic syndrome**		**T value/p value**
	Yes	**No**	
Age	48.6 ± 0.98	53.6 ± 1.37	t = 2.98**
BMI	27.76 ± 0.6	24.03 ± 0.43	t = 5.03**
Systolic BP	130.8 ± 1.99	120.98 ± 2.1	t = 3.4**
Diastolic BP	86.9 ± 1.31	80.16 ± 2.1	t = 3.4*
Fasting Sugar	203.04 ± 9.05	169.11 ± 11.9	t = 2.27*
Random Sugar	290.03 ± 10.84	256.03 ± 13.3	t = 1.92*
Triglycerides	191.82 ± 8.14	145. 54 ± 11.06	t = 3.37**
Atherogenic Index	0.61 ± 0.01	0.43 ± 0.26	t = 5.74**
Albumin	30.99 ± 2.86	25.39 ± 3.68	u = 2110.5*
Urinary albumin–creatinine ratio	75.64 ± 9.08	56.77 ± 11.2	u = 1364**

Notes: Mean ± SD, * = $p < 0.05$, ** = $p < 0.001$

3.4. Logistic Regression Analysis

Taking the presence of metabolic syndrome as a dichotomous variable, blood pressure, glucose profile, lipid profile, and diabetic complications were taken as independent covariants. The regression analysis model was found to be statistically significant with a model of variance 69% (Nagelkarke R^2), and 85.1% cases were correctly classified. Many parameters were found to significantly affect metabolic syndrome. To summarize, all the risk factors of metabolic syndrome were found to significantly affect the occurrence, such as cholesterol (Exp(B) = 1.094; $p = 0.044$), triacylglycerol (Exp (B) = 0.981; $p < 0.001$), fasting blood sugar (Exp(B) = 0.988; $p = 0.001$), systolic blood pressure (Exp(B) = 0.932; $p < 0.001$), body mass index (Exp(B) = 0807; $p = 0.001$), and presence of diabetic nephropathy (Exp(B) = 27.75; $p < 0.001$).

4. Discussion

A group of multitude of symptoms with diversified risk factors is mainly increasing with the prevalence of obesity, especially central and truncal obesity [3]. It is also termed as “insulin resistance syndrome” [2], where cells lose responsiveness to insulin because of interference in insulin signaling via inflammatory and lipid molecules [21]. Insulin resistance causes excessive fatty flux leading to precipitation of an inflammatory state,thereby increasing the risk of diabetes and hypertension [22]. According to NHLBI, metabolic syndrome is defined as obesity, hypertension, dyslipidemia, and increased sugar levels [4, 23], and the presence of at least two features confirms the presence of the disease [5].

In the present study, MS was confirmed when, in addition to diabetes, any of the two other symptoms were found, which showed that 60% (n = 93) participants presented with MS and 40% (n = 61) participants were without MS ($\chi^2 = 6.65$, $p = 0.01$)

As it is obvious from different studies the disease is mostly affected by obesity [24, 25] present study showed the same trend with an average BMI of 27.76 in MS+ subjects vs. 24.03 in MS subjects (t = 5.03, $p < 0.05$). One study also showed that men with truncal obesity have 4)% incidence rate [26]. Some studies also show that MS is more prevalent in obese patients in their fifties and sixties [27], whereas this trend in the present study was replaced by prevalence in 40s followed by 3rd and 5th decade ($\chi^2 = 95.18$, $p < 0.001$).

Metabolic syndrome has variable prevalence around the world, with as high as 63% in the Middle East [28] to as low as 10%–30% in East Asia [29] with or without diabetes. A recent study showed 70% prevalence in the sub-saharan regions of Africa [30] and 33% in Poland [31]. During 2011–16, the USA showed 34.7% prevalence with no gender difference [32]. Across Pakistan, it was found to be 18%–46% in 2008 [33]. The present study showed 60% prevalence in New Karachi Township. However, these data cannot be generalized because the study was a short-scale study.

Around the world, women are more prone to develop MS in their twenties and thirties [26, 29], but a study in Iran showed 67% female dominance in their 60s [8]. Canadian data shows 20.7% female majority

compared with 17.8% male occurrence [26, 34]. The present study was in agreement with other studies where 44% women vs 11% men ($p < 0.001$) were found to suffer from the ailment, where the most common reason may be being idle most of the time with increased sleep [35].

According to [36], the odds of occurrence of fatigue is 2.12 when presented with metabolic syndrome. In the present study, the odds of fatigue related to MS was 4.76 ($\chi^2 = 4.67$, $p < 0.001$). In some other studies, a significant correlation was found between MS and vertigo [37], which was postulated to be due to cerebral ischemic lesions precipitated by oxidative stress leading to biochemical abnormalities [38]. The present study showed the odds of vertigo to be 2.97 in relation to MS ($\chi^2 = 10.41$, $p = 0.001$). The odds of fall in MS-positive subjects was 2.12 ($\chi^2 = 4.172$, $p = 0.041$), which is consistent with [39], which reported an increased risk of fall with associated pain and inactivity in elderly obese people.

In the presence of T2DM and vasculopathy, MS is highly related to joint pain [40]. The present study is in accordance with the findings as the odds of joint pain in individuals with diabetes and MS was 3.85 ($\chi^2 = 5.21$, $p = 0.022$). Vasculopathy due to MS [41] may also lead to polyneuropathy, including pain, burning, and numbness [42]. Only peripheral burning sensation was found to be significantly correlated with the presence of MS (OR = 2.54, $\chi^2 = 5.82$, $p = 0.016$), whereas numbness (OR = 1.21) and tingling (OR = 1.3) were found to be non-significantly correlated. Diabetes patients with MS were positively correlated with diabetic neuropathy ($p < 0.05$), which is consistent with [43], which proposed a 50% prevalence of neuropathy in MS-positive patients.

According to binary logistic regression analysis, the odd of BMI >30 to present MS was 2.03, BP > 130 mmHg was 2.92 and TG > 150 mg/dl was 4.44 and fasting sugar > 125 mg/dl was 2.18. These findings were consistent with [9], which found MS 26% prevalent in US adults of >20 years of age. They identified raised BP, increased serum lipids, and broad waist as probable risk factors. The present findings also showed that MS is an independent risk factor for diabetic neuropathy as well as nephropathy, which is in accordance with the findings of [27], where MS was found to be an independent risk factor for retinopathy and nephropathy. However, this study also showed that complications such as retinopathy and neuropathy strongly depend on nephropathy, which itself depends on the presence of metabolic syndrome.

5. Conclusion

This study concludes that metabolic syndrome is 60% prevalent in the target population, mainly women. The presence of metabolic syndrome also confirms macrovascular symptoms such as joint pain and burning sensations in the lower limbs. Metabolic syndrome is an individual risk factor for neuropathy and nephropathy. To avoid the development of MS according to [44], intense lifestyle modification with or without medication is necessary, and regular medical checkups and follow-ups may decrease the occurrence and progress of complications as well as the development of insulin resistance, leading to the development of MS.

There should be awareness sessions in general hospitals for patients and their attendants so that patients can achieve their goals with lifestyle modifications.

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Abbreviations

BMI - body mass index; BP - blood pressure; Chol - cholesterol; Cr - creatinine; MS - metabolic syndrome; MS+ - metabolic syndrome positive; NHLBI - National Heart, Lung and Blood Institute; OR - odds ratio; P_{Cr} - plasma creatinine levels; SD - standard deviation; T2DM - type 2 diabetes mellitus; TG - triglycerides; TG/HDL - triglyceride/high density lipoprotein ratio; UACR - urinary albumin creatinine ratio; US - United States.

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